

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

NANOSTRING TECHNOLOGIES, INC.,)	
)	
Plaintiff,)	C.A. No. 22-1375 (MFK)
)	
v.)	
)	
10X GENOMICS, INC.,)	JURY TRIAL DEMANDED
)	
Defendant.)	
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FIRST AMENDED COMPLAINT

Plaintiff NanoString Technologies, Inc. (“NanoString” or “Plaintiff”) alleges in its First Amended Complaint for patent infringement against Defendant 10x Genomics, Inc. (“10x” or “Defendant”) as follows:

NATURE OF THE ACTION

1. This is an action for infringement of U.S. Patent Nos. 11,473,142 (the “142 Patent”), 11,377,689 (the “689 Patent”) (collectively, the “Asserted Patents”). This action arises under the patent laws of the United States, Title 35, United States Code, including U.S.C. § 271.

THE PARTIES

2. NanoString is a Delaware Corporation with its principal place of business at 530 Fairview Ave. N, Seattle, WA 98109.

3. On information and belief, 10x is a Delaware corporation with its principal place of business at 6230 Stoneridge Mall Road, Pleasanton, CA 94588.

JURISDICTION AND VENUE

4. Plaintiff incorporates by reference and restates the preceding Paragraphs 1-3 above as though fully set forth herein.

5. This civil action for patent infringement arises under the patent laws of the United States, 35 U.S.C § 1 *et seq.*, including in particular under 35 U.S.C. § 271.

6. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over Defendant, because 10x is a Delaware corporation and has purposefully availed itself of the benefits and protections of Delaware state law by incorporating under Delaware law.

8. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391 and 1400(b), because 10x is a Delaware corporation and thus resides in this District.

BACKGROUND

9. NanoString is the pioneer in the field of spatial biology. As a respected, leading innovator of translational tools, NanoString has developed and brought to market breakthrough technologies that enable scientists across the globe to envision molecular interactions in three dimensions. NanoString's GeoMx Digital Spatial Profiler ("GeoMx DSP") product is the first of its kind – it uniquely combines high-plex and high-throughput spatial profiling, which allows researchers to rapidly and quantitatively assess the biological implications of heterogeneity within tissues. Since its launch, GeoMx DSP has been amply described in prestigious scientific publications, and studies performed using GeoMx DSP have been widely presented at industry conferences.

10. On October 18, 2022, the United States Patent and Trademark Office duly and legally issued the United States Patent No. 11,473,142, entitled "Chemical Compositions and Uses

Thereof.” The named inventors of the 142 Patent are Joseph Beechem, Dae Kim, Margaret Hoang, Mark Gregory, and Erin Piazza. By operation of law and as a result of written assignment agreements, NanoString obtained the entire right, title, and interest to and in the 142 Patent. The 142 Patent is attached hereto. Ex. 1.

11. Since its issuance, NanoString has owned the 142 Patent.

12. On July 5, 2022, the United States Patent and Trademark Office duly and legally issued the United States Patent No. 11,377,689, entitled “Chemical Compositions and Uses Thereof”. The named inventors of the 689 Patent are Joseph Beechem, Dae Kim, Margaret Hoang, Mark Gregory, Erin Piazza, and Denise Zhou. By operation of law and as a result of written assignment agreements, NanoString obtained the entire right, title, and interest to and in the 689 Patent. The 689 Patent is attached hereto. Ex. 2.

13. Since its issuance, NanoString has owned the 689 Patent.

14. As the Abstract explains, the Asserted Patents are directed toward an improved and novel way of spatially detecting target analytes in regions of interest. More specifically, the method claimed in the Asserted Patents permit the simultaneous, multiplexed detection and quantification of protein and/or nucleic acid expression in a user-defined region of a tissue, cell, and/or subcellular structure within a cell, while maintaining the morphological context of the sample.

15. The claimed invention of the Asserted Patents is an improvement over prior art means of detecting target analytes in a sample. Conventional immunohistochemical methods allow for simultaneous detection of six to ten protein targets at most. Similarly, *in situ* hybridization methods are limited to less than ten nucleic acid targets. 142 Patent at 16:30-32; 689 Patent at 16:30-32. While useful, these methods do not enable the simultaneous detection of a large

number of genes, proteins, or other biologically active molecules in the same sample. Laser microdissection is able to capture many genes, but it is limited to a small number of locations and very expensive. The claimed invention of the Asserted Patents uniquely addresses and solves these problems. As such, the invention offers a spatial profiling method for RNA and/or protein in a tissue sample of much higher plex and sensitivity, providing researchers the ability to look at many biological targets at many locations in the same sample at the same time. As the Asserted Patents explain, the “present disclosure provides detection of large combinations of nucleic acid targets and/or protein targets from a defined region of a sample. The present disclosure provides an increase in objective measurements by digital quantification and increased reliability and consistency, thereby enabling comparison of results among multiple centers.” 142 Patent at 16:37-43; 689 Patent at 16:37-43. Specifically, more than 1000 targets can be detected, and “[t]here is no pre-defined upper limit to the number of regions of interest and comparisons that can be made.” 142 Patent at 16:21-23; 40:65-41:3; 689 Patent at 16:21-23; 40:61-64. Furthermore, the invention is compatible with existing, readily available sequencing technologies, making it accessible to a large number of users; it also allows for an economical assay design, as inexpensive and widely-available synthetic DNA oligonucleotides can be used instead of more expensive probes. 142 Patent at Abstract, 37:58-63; 689 Patent at Abstract, 37:50-55.

16. On information and belief, 10x launched and began shipping its commercial spatial profiling products, Visium Spatial system (“Visium”) and related products in November, 2019. See <https://www.globenewswire.com/news-release/2019/11/26/1952684/0/en/10x-Genomics-Begins-Shipments-of-Visium-Spatial-Gene-Expression-Solution.html>.

17. Visium and related products are all products, components, and services that are made, used, performed, offered to sell, sold, and/or imported in the United States by or on behalf

of 10x in connection with 10x's Visium. Visium and related products include, for example and without limitation, Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, and Certified Service Providers (CSP), that when used together allow researchers to "map the whole transcriptome within the tissue context" and "[c]ombine histological and gene expression data with easy-to-use software." See <https://www.10xgenomics.com/products/spatial-gene-expression>.

18. Visium and related products provide spatial profiling for protein and/or RNA in a tissue sample. 10x offers benchtop instrument, slides, reagents, and software for protein and RNA analysis using workflows that are compatible with standard next generation sequencing (NGS) applications. 10x markets Visium as designed to "discover and reveal the spatial organization of cell types, states, and biomarkers." See https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT059_ProductSheet_VisiumSpatialGeneExpression_Letter_digital.pdf.

Furthermore, 10x states that Visium is able to "[s]patially profile RNA expression for over 18,000 genes in human and mouse FFPE samples with high resolution across entire tissue sections," see https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT000128_PS_Spatial_biology_without_limits_Spatial_gene_expression_in_FFPE.pdf, offers "tissue profiling with transcriptomics and protein co-detection," see <https://www.10xgenomics.com/products/spatial-proteogenomics>, allows users to "define regions of interest," see https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT088_RevA_ProductSheet_Immunofluorescence%20Capability_Letter_digital.pdf, and is "[e]asy to integrate with current histological laboratory methods and tools for tissue analysis." *Id.*

19. 10x practices the Asserted Patents by using Visium and related products on behalf of its own scientists, researchers, and its Visium customers for various purposes, including without limitation research, development, sales, and support.

20. 10x infringes the Asserted Patents by providing customers with Certified Service Providers (CSP), who offer support for complete end-to-end Visium workflows and perform various tasks, from sample preparation to library generation to data processing, for its customers. See <https://www.10xgenomics.com/service-providers?query=&page=1>.

21. 10x additionally infringes the Asserted Patents by making, using, selling, offering for sale, importing into the United States, and supplying from the United States the patented inventions and/or its components, including without limitation Visium, Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, and CSP.

22. Through the development and subsequent making, using, selling, offering for sale, importing and exporting of its Visium and related products, and performing every step of the patented invention by using products, services, devices, systems, and/or components of the systems that embody the patented inventions, such as Visium and related products, 10x has and continues to directly infringe, contributorily infringe, and/or induce the infringement of the Asserted Patents.

COUNT I

Infringement of U.S. Patent No. 11,473,142 by 10x

23. NanoString incorporates by reference and restates the preceding Paragraphs 1-22 above as though fully set forth herein.

24. 10x has infringed and continues to directly infringe one or more claims of the 142 Patent, including without limitation claims 1-13, pursuant to 35 U.S.C. § 271(a), literally or under

the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority all products, components, and services in connection with 10x's Visium, including without limitation Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization software, Space Ranger and Loupe Browser, CSP, and other products and services sold by 10x for use in 10x's Visium workflows.

25. To demonstrate how 10x infringes one or more claims of the 142 Patent, attached is a preliminary and exemplary infringement claim chart. Ex. 3. This chart is not intended to limit NanoString's right to modify this chart or any other claim chart or allege that other activities of 10x infringes the identified claims or any other claims of the 142 Patent or any other patents. This chart is hereby incorporated by reference in its entirety. Each claim element that is mapped to Visium and related products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

26. 10x has actively induced and continues to induce the infringement of one or more claims of the 142 Patent, including without limitation claims 1-13, pursuant to 35 U.S.C. § 271(b) through a range of activities, including without limitation making and selling Visium and related products; controlling the design, manufacture, and supply of materials, software, and instruments to be used with Visium and related products; substantially marketing Visium and related products; intentionally instructing or otherwise encouraging others, including 10x's customers and end users, to use the infringing products in the United States in the manner that infringes one or more claims of the 142 Patent; creating distribution channels for the infringing products; and supporting the sale of those products in the United States. As an example, 10x implemented Certified Service Provider (CSP) program to promote, service, and sell the infringing products domestically. As a

further example, 10x distributes Visium and related products promotional and marketing materials and Visium and related products User Manuals in websites directed to the United States Market.

27. 10x has contributed and continues to contribute to the infringement of one or more claims of the 142 Patent, including without limitation claims 1-13, pursuant to 35 U.S.C. § 271(c) through a range of activities, including without limitation, without authority, importing into the United States materials and instruments that are material components of the claimed inventions of the 142 Patent; without authority, importing into the United States materials and instruments for practicing the patented method of the 142 Patent; selling and/or offering for sale Visium and related products, or has others perform such acts on its behalf; and instructing users of 10x's Visium workflows to directly infringe one or more claims of the 142 Patent. Visium and related products are specifically designed to be used in an infringing manner, where no non-infringing use of Visium and related products has been described in 10x's instructional materials. Therefore, 10x's Visium and related products constitute a material part of the claimed invention of the 142 Patent, and are not a staple article or commodity of commerce suitable for substantial non-infringing use. As an example, 10x supplies in the United States products specifically designed for use in practicing one or more claims of the 142 Patent, including for example the Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, Space Ranger, and Loupe Browser and threaten to sell those products throughout the United States.

28. 10x has had knowledge of US Patent Publication US 2021/0403999 published on December 30, 2020 that lead to the issuance of the 142 Patent since at least October 12, 2022, the date when 10x specifically questioned Margaret Hoang, a 30(b)(6) witness in a separate case before this Court, 1:22-cv-00261-MFK, about the aforementioned Patent Publication prior to the issuance of the 142 Patent, demonstrating clear effort by 10x to actively track NanoString's

intellectual property estate. On information and belief, 10x became aware of the 142 Patent on October 18, 2022, the date of its issuance. Furthermore, 10x was served with NanoString's Complaint, along with detailed infringement claim chart applying the 142 Patent to 10x's products, on October 20, 2022. On information and belief, 10x's outside counsel subsequently reviewed NanoString's Complaint with 10x's internal legal personnel, and 10x has affirmatively decided to continue infringing. At the very least, service of NanoString's Complaint on October 20, 2022 provided 10x with not just notice of the 142 Patent, but also 10x's ongoing infringement of the 142 Patent. 10x's infringement since October 20, 2022 has been willful.

29. NanoString has suffered and continues to suffer damages as a result of 10x's infringement of the 142 Patent.

30. Unless 10x is enjoined from infringing the 142 Patent, 10x's efforts to design, develop, market, offer to sell, and sell Visium and related products will cause NanoString to suffer irreparable injury for which damages are an inadequate remedy.

COUNT II

Infringement of U.S. Patent No. 11,377,689 by 10x

31. NanoString incorporates by reference and restates the preceding Paragraphs 1-30 above as though fully set forth herein.

32. 10x has infringed and continues to directly infringe one or more claims of the 689 Patent, including without limitation claims 16, 21, 24, 27, 30, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority all products, components, and services in connection with 10x's Visium, including without limitation Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and analysis and visualization

software, Space Ranger and Loupe Browser, CSP, and other products and services sold by 10x for use in 10x's Visium workflows.

33. To demonstrate how 10x infringes one or more claims of the 689 Patent, attached is a preliminary and exemplary infringement claim chart. Ex. 4. This chart is not intended to limit NanoString's right to modify this chart or any other claim chart or allege that other activities of 10x infringes the identified claims or any other claims of the 689 Patent or any other patents. This chart is hereby incorporated by reference in its entirety. Each claim element that is mapped to Visium and related products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

34. 10x has actively induced and continues to induce the infringement of one or more claims of the 689 Patent, including without limitation claims 16, 21, 24, 27, 30, pursuant to 35 U.S.C. § 271(b) through a range of activities, including without limitation making and selling Visium and related products; controlling the design, manufacture, and supply of materials, software, and instruments to be used with Visium and related products; substantially marketing Visium and related products; intentionally instructing or otherwise encouraging others, including 10x's customers and end users, to use the infringing products in the United States in the manner that infringes one or more claims of the 689 Patent; creating distribution channels for the infringing products; and supporting the sale of those products in the United States. As an example, 10x implemented Certified Service Provider (CSP) program to promote, service, and sell the infringing products domestically. As a further example, 10x distributes Visium and related products promotional and marketing materials and Visium and related products User Manuals in websites directed to the United States Market.

35. 10x has contributed and continues to contribute to the infringement of one or more claims of the 689 Patent, including without limitation claims 16, 21, 24, 27, 30, pursuant to 35 U.S.C. § 271(c) through a range of activities, including without limitation, without authority, importing into the United States materials and instruments that are material components of the claimed inventions of the 689 Patent; without authority, importing into the United States materials and instruments for practicing the patented method of the 689 Patent; selling and/or offering for sale Visium and related products, or has others perform such acts on its behalf; and instructing users of 10x's Visium workflows to directly infringe one or more claims of the 689 Patent. Visium and related products are specifically designed to be used in an infringing manner, where no non-infringing use of Visium and related products has been described in 10x's instructional materials. Therefore, 10x's Visium and related products constitute a material part of the claimed invention of the 689 Patent, and are not a staple article or commodity of commerce suitable for substantial non-infringing use. As an example, 10x supplies in the United States products specifically designed for use in practicing one or more claims of the 689 Patent, including for example the Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, Space Ranger, and Loupe Browser and threaten to sell those products throughout the United States.

36. 10x has had knowledge of the 689 Patent since at least July 11, 2022, the date when 10x was notified of NanoString's intent to add a counterclaim of infringement of U.S. Patent 11,377,689 to the 22-cv-261 litigation. Furthermore, 10x received NanoString's proposed amended counterclaims, along with detailed infringement claim chart applying the 689 Patent to 10x's products, on July 19, 2022. On information and belief, 10x's outside counsel subsequently reviewed NanoString's amended pleadings with 10x's internal legal personnel, and 10x has affirmatively decided to continue infringing. At the very least, service of NanoString's proposed

amended counterclaim on July 19, 2022 provided 10x with not just notice of the 689 Patent, but also 10x's ongoing infringement of the 689 patent. 10x's infringement since this time has been willful.

37. NanoString has suffered and continues to suffer damages as a result of 10x's infringement of the 689 Patent.

38. Unless 10x is enjoined from infringing the 689 Patent, 10x's efforts to design, develop, market, offer to sell, and sell Visium and related products will cause NanoString to suffer irreparable injury for which damages are an inadequate remedy.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully request that the Court enter the following relief in its favor and against 10x:

- A. That this Court enter judgement that Defendant has infringed and continues to infringe one or more claims of the Asserted Patents, either literally or under the doctrine of equivalents;
- B. That this Court enter judgment that Defendant's infringement has been willful;
- C. That this Court enter an order enjoining Defendant, and its officers, directors, agents, servants, affiliates, employees, divisions, branches, subsidiaries, parents, assigns and successors in interest, and all others acting in active concert therewith, including related individuals and entities, customers, representatives, distributors, and dealers, from further infringement of the Asserted Patents. In the alternative, if the Court finds that an injunction is not warranted, NanoString requests an award of post-judgement royalty to compensate for future infringement;
- D. An award of all monetary relief adequate to compensate for damages resulting from Defendant's infringement, including lost profits but in no event less than a reasonable

royalty under 35 U.S.C. § 284 for Defendant's infringement, including all pre-judgment and post-judgment interest at the maximum rate allowed by law;

- E. That this Court enter a judgment declaring this case exceptional under 35 U.S.C. § 285 and awarding NanoString its attorneys' fees and prejudgment and post-judgment interest;
- F. That this Court award NanoString all of its costs of this action; and
- G. That this Court grant such other and further relief as the Court shall deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Plaintiffs hereby demand a jury trial on all issues so triable.

Dated: January 27, 2023

Respectfully submitted,
FARNAN LLP

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